[redacted]
Michigan Medicine, University of Michigan
Paul Cederna, MD

Re: Written Feedback for High density Interconnects with Variable Electronics (HIVE) Recording Module

This document is being communicated via e-mail as an attachment. The date on which the Food and Drug Administration (FDA) sent this e-mail is the official date of this correspondence.

This document contains the FDA's written feedback to your Pre-Submission request. This feedback represents our best advice based on the information provided in the Pre-Submission and other information currently known. While our review of your Pre-Submission does not imply that your future submission will necessarily be approved or cleared, FDA intends that this feedback will not change, provided that the information submitted in a future IDE or marketing application is consistent with that provided in this current Pre-Submission and that the data in the future submission do not raise any important new issues materially affecting safety or effectiveness.

If you requested a meeting and this feedback satisfies your needs, you may cancel our upcoming meeting by contacting the lead reviewer. If you still wish to meet, please provide us with your agenda of items and any slides you wish to present no later than two business days prior to the scheduled meeting date per the Pre-Submission Guidance https://www.fda.gov/media/114034/download. If that agenda or presentation contains significant new information, FDA may not be prepared to discuss it. As a reminder, you are expected to submit draft meeting minutes as an amendment to this pre-submission within 15 days of the meeting.

Our feedback to your pre-submission questions is provided below.

Sponsor Question

1. The greatest safety risk of the HIVE recording module itself is the potential for electrical harm to the patient. We believe that this is sufficiently mitigated by testing the design for leakage current and our manufacturing plan. Does the FDA concur with this statement?

Official FDA Response

You specify that the potential for electrical harm to the patient is sufficiently mitigated by testing the design for leakage current and your current manufacturing plan. Although we agree that this approach is sound for scenarios where leakage current does not result in harm and the direct current density on any conductive surface or electrode does not exceed 0.75 $\mu A/mm^2$ for the investigational device exemption (IDE) studies, we are concerned for potential harm to patients due to heating. As noted in the *ISO 14708-1* standard, the unintended heat generated at an active implant location should not exceed 2°C. Therefore, we recommend that you evaluate the generated heat at the active implant region via bench testing and provide this assessment in your future IDE Supplement. We also recommend that you include a plan for monitoring adverse events related to heating in your future protocol to ensure adverse events that may result from heating are adequately captured.

Sponsor Question

2. We believe the risk of damage to the HIVE recording module due to electrostatic discharge is mitigated since the amplifier contains ESD protection and is only handled in controlled environments. Does the FDA concur with this statement?

Official FDA Response

You specify that the risk of damage due to electrostatic discharge (ESD) is mitigated given that the amplifier contains internal ESD diodes that protect against mild ESD events (see page 8 of 28 in document *002_Pre Submission Packet*). However, as you have assessed, this only addresses mild ESD events and does not adequately address the risk of damage due to high ESD events. The ESD levels anticipated in the intended use environment can reach up to ± 15 kV. Therefore, we do not agree that the risk of damage due to ESD to the HIVE recording module is mitigated from the amplifier selection. However, for the noted early feasibility study (EFS), we agree that if the recording module is non-functional due to an ESD event, replacing the recording module and connecting it to the Networked Neuroprosthesis (NNP) and percutaneous electrodes is an appropriate mitigation. In your future submission, we recommend that the risk of harm to a patient when discharge beyond the limit of the diode reaches the patient be evaluated as part of the risk-profile of the investigational device. We also recommend that your protocol be updated to include methods to record such events as adverse events and present these as part of your study results and reports.

Sponsor Question

3. Overall, the system components are the same (electrodes, prosthetic hand) or have the same function (wearable HIVE recording module, Smart Link Controller) as devices currently used under our IDE in supervised settings. We believe the attached hazards analysis of the wearable HIVE recording module and this document sufficiently capture the risks of the existing and new devices. Are there any other risks we should think about for use in a supervised research setting?

Official FDA Response

You specify in your device description outlined on page 6 of 28 (see document *002_Pre Submission Packet*) that you intend to add the High density Interconnects with Variable Electronics (HIVE) recording module as an additional study device to your ongoing investigational device exemption [redacted]. You note that the HIVE recording module is part of a larger future implantable system, the COSMIIC, which is based on the architecture of the Networked Neuroprosthesis (NNP) currently utilized as part of IDE[redacted]. You specify that the HIVE recording module will first be utilized to provide intuitive functional control of multi-articulated prosthetic hands. The wearable system that you intend to add to your ongoing IDE will be composed of the following elements:

1. Percutaneous [redacted] electrodes (currently utilized as part of [redacted])
2. HIVE recording module
3. Wearable NNP power module (currently utilized as part of [redacted])
4. Smart link controller (SLC) and socket
5. Prosthetic hand (currently utilized as part of [redacted])

Based on the information provided in your current supplement, the components that have not yet been FDA cleared/granted/approved for marketing, or approved for use as part of an ongoing IDE for similar use, may require testing to support safe use unless valid scientific rationale is provided to demonstrate device safety for the proposed use. Therefore, we provide the following recommendations for your consideration:

a. You provided a risk analysis for many of the components that make up the wearable HIVE recording module. However, we could not locate a risk associated with the HIVE recording module immunity to unintended non-ionizing electromagnetic fields. Electromagnetic compatibility is the device's responses when exposed to electromagnetic (EM) fields expected in the intended use environment. The electromagnetic environment has changed since previously evaluated in your IDE study due to emerging technology, and there is a possibility that electromagnetic fields may induce current on the lead wires which may result in unintended current flow resulting in harm to the patient or unintended arm movement resulting in patient harm. Therefore, we recommend that you provide an updated risk-analysis of the electromagnetic phenomena that can occur in your intended use environment(s) in your future IDE Supplement.
b. You specify that the system components are the same (electrodes, prosthetic hand) or have the same function (wearable HIVE recording module, Smart Link Controller) as devices currently used under your IDE in supervised settings. You note that the hazard analysis of the wearable HIVE recording module and this document sufficiently capture the risks of the existing and new devices. However, although the Networked Neural Prosthesis (NNP) is an IDE approved device, it will still be important for you to specify the risks and mitigations of use as it relates to your particular study. Therefore, we recommend that you also include risks and mitigations of use for this device in your future IDE Supplement for our review.
c. In your current submission, you propose additional devices that will likely require changes to your software. However, it is unclear what software changes will be implemented as part of the proposed device changes. Although it is not expected that you provide complete software documentation according to your device's level of concern as part of your IDE, we do recommend that you provide any changes in risks, and potential issues that you expect to occur as a result of the proposed device changes.

   As noted above, although complete software documentation is not currently required, we recommend that you consider utilizing the guidance, *Content of Premarket Submissions for Device Software Functions* (https://www.fda.gov/media/153781/download) for reference as you evaluate risks related to your device's software.

Please note that given that no clinical protocol has been provided, recommendations may change depending on what protocol changes are specified in the future.

Sponsor Question

4. The HIVE recording module electronics will be manufactured to a rigorous standard (flying probe PCB test, IPC Class 3) from commercial vendors (Excello, Screaming Circuits). From there the devices are shipped to University of Michigan where each device will be programmed and benchtop tested with the power module before human use. We believe this sufficiently minimizes the risk of manufacturing errors. Does the FDA concur with this statement?

Official FDA Response

You ask whether we concur that your current approach to manufacturing the HIVE recording module minimizes the risk of manufacturing errors for the device. Please note that only one approach was provided in your submission for consideration. However, given that device changes are expected throughout the course of an investigational device exemption (IDE) early feasibility study (EFS), your proposed

manufacturing process may minimize the risk of manufacturing errors for a device whose design has not been completely finalized.

As specified in Section 9 of the guidance document, *Investigational Device Exemptions (IDEs) for Early Feasibility Medical Device Clinical Studies, Including Certain First in Human (FIH) Studies* (https://www.fda.gov/media/81784/download), "When complying with the requirements of 21 CFR 820.30 under an IDE, a device manufacturer shall establish and maintain a plan that describes or references the design and development activities specific to the medical device being designed or manufactured. This plan does not need to be submitted in the IDE application. The design plan shall describe or reference the following design and development activities in accordance with 21 CFR 820.30.

- Definition of responsibility for the implementation of the design and developmental activities;
- Identification and description of the interfaces with different groups or activities that provide or result in input to the design development process;
- Verification that the design outputs that are essential for the proper functioning of the device were identified;
- Formulation of a plan to conduct design reviews to assess the progress of the design, and confirm the design is ready to move to the next phase of development;
- Assurance that the design outputs met the design input requirements as part of the design verification;
- Completion of a design validation to show that the approved design met the predetermined user needs and intended uses;
- Performance of a risk analysis and consideration of risk throughout the design process;
- Documentation and control of design changes occurring during pre-production and post-production of the device; and
- Documentation of the design transfer into production specifications.

Appropriate documentation and establishment of the aforementioned elements of the device design plan will facilitate meeting the design control requirements in 21 CFR 820.30 as the device design evolves."

Therefore, as specified above, although your manufacturing plan that describes or references the design and development activities specific to your investigational device is not required in your future IDE Supplement, we recommend that you provide a summary statement outlining your design controls to meet the requirements of 21 CFR 820.30.

Although our review focused on addressing the questions you asked, in the course of reviewing your pre-submission, we also noted the following. This is not intended to be an exhaustive list of issues.

1. On page 23 of 28 of submission document *002_Pre Submission Packet*, you specify that "[t]he first secondary objective of the study is to assess the efficacy of the electrodes in recording electromyographic signals from the RPNI grafts. The second secondary objective of IDE G160229 is to assess the efficacy of the electrodes in delivering electrical stimulation to the RPNI grafts to evoke sensory percepts." However, on page 7 of 28, you note that the wearable system proposed does not contain any stimulation modules. Therefore, it is unclear how the secondary objective or endpoint related to the effects of stimulation will be assessed if the proposed device cannot stimulate. Thus, we recommend that you refine

the secondary objectives, or provide clarity on how each study device relates to the specified study objectives.

2. On page 19 of 28 of your submission, you specify that the HIVE recording module will be connected to the percutaneous bipolar electrode leads and mounted on the patient's arm. However, is unclear whether the leads/wires will be secured to avoid potential forces that could damage the wires and potentially lead to bleeding or irritation at the lead exit site. Because this is a patient safety concern, we recommend that you ensure that all wires that could potentially be damaged due to tugging/pulling/forces are appropriately secured to mitigate the aforementioned concerns in your future protocol.

This notification is being sent in lieu of a formal written letter. If you have any questions, please contact [redacted]